REMARKS

Claims 15-34 are pending following entry of the amendment presented above. Claims 28-34 have been added, and Claims 15, 16, 19, 20 and 23-26 amended. Pages 7 and 8 of the specification have been amended to add sequence identifiers. The marked up version of the amendments to the specification and claims is attached hereto and is captioned "Version with Markings to Show Changes Made."

The outstanding issues will be addressed below in the order raised in the outstanding Office Action of June 4, 2002.

I. Election/Restriction.

The Examiner has maintained the Restriction Requirement and made it final, stating that the "claims have been examined to the extent that they are limited to methods which detect EBNA-1 and BARF-1 sequences and to the primers of SEQ ID NO:2 and 3 and probe of SEQ ID NO:5 for the detection of EBNA-1 and the primers of SEQ ID NO:23 and 24 and the probe of SEQ ID NO:26 for the detection of BARF-1." (Office Action, page 3, lines 3-6). The Examiner has required that the claims directed to LMP-2 nucleic acids be canceled or amended to delete any recitation of the LMP-2 nucleic acids. Although Applicants respectfully disagree with this rejection, the claims as amended do not recite LMP-2 sequences.

The Office Action further indicates that only the BKRF1 and BARF1 sequences of SEQ ID NOS: 2, 3, 5, 23, 24 and 26 will be examined, and that SEQ ID NOS: 1, 4, 22 and 25 will not be examined. The Examiner states that it would be an undue burden to examine both Claim 19 and the specific sequences recited in the claims that depend from Claim 19.

Applicants have amended the claims to omit recitation of SEQ ID NOS: 1 and 4 (BKRF1), but have maintained SEQ ID NOS: 22 and 25 (BARF1) on the basis that at such time as Claim 19 is found to be allowable over the art, these claims will also be allowable.

II. Sequence Listing.

The application stands objected to for failing to comply with the rules regarding applications that contain nucleotide and/or amino acid sequences as set forth in 37 C.F.R. § 1.821 – § 1.825 on the basis that the Sequence Listing does not include all of the sequences recited in the Specification. Specifically, the Office Action states that the Sequence Listing does not include the sequence of the T7 polymerase promoter (citing Claims 16 and 23).

Applicants apologize for this oversight and any inconvenience it caused the Examiner in searching and examining the claims. Claims 16 and 23, as well as the Specification at pages 7-8, have been amended to add a sequence identifier to identify the sequence of the T7 polymerase promoter. New paper and computer readable copies of the Sequence Listing are submitted concurrently herewith.

Applicants submit that this application is now in compliance with the provisions of 37 C.F.R. § 1.821 – § 1.825, and respectfully request that the objection on this basis be withdrawn.

III. Informalities in the Claims.

The claims stand objected to for informalities on several grounds. First, the Office Action states that Claim 15 contains a typographical error and "fro" should be "from." This language has been omitted from Claim 15 as rewritten, thereby obviating this objection.

Claims 25 and 26 are objected to on the basis that Claim 25 does not properly depend from Claim 15, as a product claim cannot depend from a method of using the product. Claim 25 has been rewritten so that it no longer depends from Claim 15.

Claims 20, 23 and 24 stand objected to for failure to properly recite a Markush group. Claims 20 and 23 have been amended as suggested; however, in view of other amendments to Claim 24, this claim no longer recites a Markush group.

In view of the foregoing, Applicants submit that the informalities in the claims have been addressed, and request that the outstanding objections be withdrawn.

IV. Section 112, first paragraph.

Claims 15-18 stand rejected under 35 U.S.C. § 112, first paragraph, the Examiner stating that "the specification, while being enabling for methods of detecting EBV positive NPC or gastric carcinoma cells . . . does not reasonably provide enablement for methods which detect any EBV positive epithelial tumor cell." (Office Action, page 4, point 4, lines 1-6).

Although Applicants respectfully disagree with this rejection, Claims 15 and 25 have been amended to recite "nasopharyngeal carcinoma or gastric carcinoma cells" to expedite the prosecution of this application to allowance in accordance with USPTO Patent Business Goals (65 Fed. Reg. 54603, September 8, 2000) without prejudice to the filing of a continuation application.

In view of the foregoing, Applicants submit that the amendments to Claims 15 and 25 have addressed the outstanding rejection, and respectfully request that the outstanding enablement rejection be withdrawn.

V. Section 112, second paragraph.

The claims stand rejected on various grounds of indefiniteness. These rejections will be addressed individually below.

A. Claims 15-18.

Claims 15-18 stand rejected on the basis that Claim 15 does not recite a step of detecting the amplified EBNA-1 and BARF-2 nucleic acids. Claim 15 has been amended to more clearly recite detecting the presence or absence of amplified target sequences, where the presence of EBV-positive NPC or gastric carcinoma cells is determined by the presence of the amplified target sequences.

In addition, new Claim 28 has been added which further recites an optional step of detecting the presence or absence of the amplification products of the amplification reaction of step (a).

It is noted for the record that in the claimed methods the amplifying and detecting steps may be carried out serially or simultaneously as would be appreciated by those skilled in the art.

B. Claim 16.

Claim 16 stands rejected as indefinite for lack of proper antecedent basis for the recitation of "the pairs of oligonucleotides." Claim 16 has been amended as suggested by the Examiner to address this rejection. In addition, Claim 16 has been amended to remove the Markush language. Claim 16 is directed to a method wherein the first set of primers is used in step (a) and the second set of primers is used in step (b). Thus, the Markush group language has been omitted to more clearly recite the features of the invention.

Claim 16 has further been amended to clarify that the oligonucleotides may contain elements other than the EBNA-1 specific sequences (such as the T7 promoter sequence recited by the claim).

C. Claims 16 and 23.

Claims 16 and 23 stand rejected as indefinite for recitation of "provided with a T7 promoter sequence", the Examiner stating that it is not clear whether the T7 promoter sequence is provided separately with the pair of oligonucleotides or whether one or both of the primers further comprises the T7 promoter.

Applicants note that the T7 promoter sequence is a non-hybridizing part of the primer and, according to the methods of Claims 16 and 23, is not provided as a separate sequence. Claims 16 and 23 have been amended to more clearly recite that the claimed method involves the use of a primer pair, wherein at least one of the primers in each primer pair (SEQ ID NO:3 and SEQ ID NO:24) comprises the T7 promoter sequence.

D. Claims 19-22 and 24-26.

Claims 19-22 and 24-26 stand rejected as indefinite for the recitation of the term "corresponding", the Office Action stating that "this is not an art recognized term to describe the relationship between two nucleic acid sequences." Claim 19 has been rewritten to omit much of the preamble, including the term "corresponding", on the basis that the deleted language is superfluous.

E. Claim 25 – "substantially complementary".

Claim 25 stands rejected as indefinite for reciting "a nucleic acid sequence substantially complementary" to the amplified sequence, the Office Action stating that the "specification does not provide a definition for this phrase and there is no art recognized definition for the term "substantially". (Office Action, sentence spanning pages 7-8).

Claim 25 has been amended to omit the language reciting a probe, and new Claim 28 has been added, which depends from Claim 25 and recites a probe that is substantially complementary to and can hybridize to the amplified nucleic acid sequence.

Applicants submit that the recited language "substantially complementary" is not unclear in view of the extensive knowledge in the art as to the function of a probe. It would be appreciated by those of ordinary skill in the art that the function of a probe is to hybridize to the target, but that complete complementarity between the probe and the target sequence is not required. Thus, one of ordinary skill in the art would be able to appreciate the metes and bounds of an oligonucleotide that is "substantially complementary" to a target sequence and functions as a probe.

F. Claim 25 – "the amplified nucleotide sequence".

Claim 25 further stands rejected on the basis that the term "the amplified nucleic acid sequence" lacks proper antecedent basis. This language has been deleted from Claim 25, thereby obviating this rejection.

G. Claim 26.

Claim 26 stands rejected as indefinite for reciting a "test kit according to claim 24" on the basis that claim 24 does not recite a test kit. Claim 26 has been amended to depend from new Claim 28 to provide proper claim dependency.

In view of the foregoing, it is submitted that the pending claim set satisfies the requirements of § 112, second paragraph, and it is respectfully requested that the outstanding indefiniteness rejections be withdrawn. It is noted for the record that none of the amendment discussed above narrow the scope of the claims.

VI. Rejections under § 102.

Claims 19 and 20 stand rejected on several grounds of anticipation over Cheung et al. and Myers. These rejections are addressed individually below.

A. Cheung et al.

Claim 19 stands rejected under 35 U.S.S. § 102(b) as anticipated by Cheung et al. The Office Action states that Cheung et al. discloses primers for amplifying BKRF1 which primers are encompassed by the BKRF1 reading frame spanning nucleotides 107950 – 109872. Claim 19 has been amended to omit reference to the BKRF1 reading frame spanning nucleotides 107950 – 109872. Accordingly, it is respectfully requested that the outstanding anticipation rejection be withdrawn.

B. Claims 19 and 20 – (GenBank Accession No. G34340).

Claims 19 and 20 stand rejected under 35 U.S.C. § 102(a) as anticipated by Myers (GenBank Accession No. G34340). The rejection appears to be on the basis that a portion of one of the primers disclosed in the

cited reference corresponds to 10 nucleotides of SEQ ID NO:23. Claims 19 and 20 have been amended to recite that the oligonucleotide is at least "15-35 nucleotides in length" and comprises "at least a fragment of 15 nucleotides" from the recited sequences. Support for the recitation of 15 nucleotides as a minimum length for the oligonucleotide is found in the specification at page 8 (lines 29-30), which recites: "Usually primers contain about 15-26 nucleotides but longer primers may also be employed."

The sequences of SEQ ID NO:22, SEQ ID NO:24 and SEQ ID NO:25, which are free of the rejection over Myers have been deleted from Claim 20 and incorporated into a new Claim 32, which retains the language "at least a fragment of 10 nucleotides".

Moreover, as Claim 19 no longer recites EBNA-1 sequences, SEQ ID NO:2 and SEQ ID NO:3 have been omitted from Claim 20, and new Claim 29 has been added, which recites SEQ ID NO:2 and SEQ ID NO:3, as well SEQ ID NO:5 (also an EBNA-1 sequence).

Myers does not disclose an oligonucleotide comprising at least 15 nucleotides of the sequences recited by Claims 19 and 20. Moreover, the recited sequences would not have been obvious in view of the oligonucleotides of Myers.

The Examiner has further rejected Claim 20 as "inclusive of sequences sharing any level of sequence complementarity" to the recited sequences. Applicants respectfully disagree with this rejection which has absolutely no basis in the understanding of those skilled in the art regarding the meaning of the term "complementary".

In view of the foregoing discussion, it is requested that the outstanding rejection under § 102(a) be withdrawn.

C. Claim 19 -- (GenBank Accession No. G29936).

Claim 19 further stands rejected under 35 U.S.C. §102(a) as anticipated by Myers (GenBank Accession No. G29936), which the Office Action states discloses a 10 nucleotide fragment of SEQ ID NO:26. This

rejection has been addressed as discussed in the previous section by amending Claims 19 and 20 to recite that the oligonucleotide is at least "15-35 nucleotides in length" and comprises "at least a fragment of 15 nucleotides" from the recited sequences.

Moreover, new Claim 34, which specifically recites SEQ ID NO:26 also recites "at least a fragment of 15 nucleotides." SEQ ID NO:26 was previously found in Claim 24.

As Myers does not disclose or suggest the recited sequences of amended Claim 19, it is respected that the outstanding rejection be withdrawn.

VII. Rejections under § 103(a).

The claims stand rejected on a number of grounds of obviousness. The various rejections will be addressed individually below.

A. Cheung et al.

Claim 25 stands rejected for obviousness over Cheung et al. The Examiner states that Cheung et al. discloses primers of 19-21 nucleotides for amplifying BKRF1 within the region spanning nucleotides 107950 – 109872. The Office Action further states that labeled probes are known. The Office Action concedes that the cited reference does not disclose a kit. The Office Action states, however, that the claimed kit would have been obvious.

Although Applicants respectfully disagree with this rejection, as discussed above with respect to the rejection under §102, Claims 19-22 and 24 (from which Claim 25 depends) have been amended to omit recitation of the BKRF1 reading frame spanning nucleotides 107950 – 109872. New Claims 32 and 33, from which Claim 25 also depends do not recite BKRF1 sequences. Claims 29 and 30 recite SEQ ID NO:2 and SEQ ID NO:3, as well as SEQ ID NO:5, which are sequences from the BKRF1 reading frame of EBNA-1; however, these particular sequences are not disclosed or suggested by Cheung et al.

In sum, the oligonucleotides recited by Claim 25 are neither disclosed nor suggested by Cheung et al. It is therefore respectfully requested that the outstanding rejection under § 103 (a) be withdrawn.

B. Claim 24 -- Myers (GenBank Accession No. G29936).

Claim 24 stands rejected under §103 (a) as unpatentable for obviousness over Myers (GenBank Accession No. G29936). It is unclear whether this rejection is over Myers alone or Myers in combination with Mullis. The Office Action states that Myers discloses a primer comprising at least 10 nucleotides of SEQ ID NO:26 (derived from BARF1) and that Mullis teaches the use of labeled primers for PCR. Accordingly, the Examiner states it would have been obvious to combine the oligonucleotide of Myers with a detectable label.

Claim 24 has been amended to remove the language reciting the detectable label, *i.e.*, when the oligonucleotide is used as a non-labeled primer. New Claim 31 has been added which further recites the labeled probe.

As discussed above with respect to the anticipation rejection of Claim 19 over Myers, Claim 19 (from which Claim 24 depends) has been amended to recite an oligonucleotide of at least 15-35 nucleotides in length where the oligonucleotide comprises a fragment of at least 15 nucleotides of the BARF1 reading frame spanning nucleotides 165504-166166. As Myers does not disclose or suggest the recited oligonucleotides, it is respectfully requested that the outstanding obviousness rejection be withdrawn.

With respect to new Claim 31, which specifically recites SEQ ID NO:5, Myers does not disclose or suggest this sequence. New Claim 31 is therefore also free of the Myers reference.

C. Cheung in view of Kievits.

Claim 21 stands rejected for obviousness over Cheung and Kievits, the Office Action stating that Cheung discloses primers for amplifying BKRF1

sequences within the EBV region 107950 – 109872 as well as labeled probes. The Office Action concedes that Cheung et al. does not disclose incorporating a T7 polymerase promoter in the primer, but states that Kievits teaches primers modified to include T7 promoter sequences for NASBA.

As discussed above, Claim 19 (from which Claim 21 depends) has been amended to omit recitation of BKRF1 sequences. Accordingly, the Applicants submit that Cheung et al., taken alone or in combination with Kievits, does not disclose or suggest the claimed oligonucleotide, and request that the outstanding obviousness rejection be withdrawn.

D. Claims 21 and 22 – Myers (GenBank Accession No. G34340) in view of Kievits.

Claims 21 and 22 stand rejected under 35 U.S.C. § 103(a) as unpatentable for obviousness over Myers (GenBank Accession No. G34340) in view of Kievits. This rejection is respectfully traversed below.

The Office Action states that Myers discloses a primer comprising at least 10 nucleotides of SEQ ID NO:23 (BARF-1). As discussion in the context of the § 102 rejections, Claims 19 and 20 have been amended and new Claim 32 added to distinguish the claimed invention from Myers.

Applicants submit that Myers, taken alone or in combination with Kievits, does not render obvious the subject matter of Claims 21 and 22, and respectfully request that the rejection on this basis be withdrawn.

E. Claim 21 – Myers (GenBank Accession No. G29936) in view of Kievits.

Claim 21 stands rejected under 35 U.S.C. § 103(a) as unpatentable for obviousness over Myers (GenBank Accession No. G29936) in view of Kievits. This rejection is respectfully traversed below.

The Office Action states that Myers discloses a primer comprising at least 10 nucleotides of SEQ ID NO:26 (BARF-1). As discussed in the context of the § 102 rejections, Claim 19 (from which Claim 21 depends) has been

amended to distinguish the claimed invention from Myers. With respect to new Claim 34, which specifically recites SEQ ID NO:26, this claim also recites "at least a fragment of 15 nucleotides", which distinguishes the claimed subject matter from the cited references.

Accordingly, Applicants submit that the subject matter of Claim 21 is nonobvious over Myers, taken alone or in combination with Kievits, and respectfully request that the outstanding obviousness rejection be withdrawn.

F. NCBI (Accession No. M80517) in view of Zhang et al. and Cheung et al.

Claims 19, 20, 24, 25 and 26 stand rejected under 35 U.S.C. § 103(a) as unpatentable for obviousness over NCBI (Accession no. M80517) in view of Zhang et al. and Cheung et al. The Office Action states that the NCBI sequence discloses the complete sequence of the EBV genome, including the BARF-1 reading frame. The Office Action concedes that NCBI does not teach primers or probes from within the BARF-1 open reading frame. The Office Action further states that Zhang et al. discloses a probe comprising the complete BARF-1 sequence labeled with a detectable moiety, and that BARF-1 expression is correlated with the occurrence of lymphomas. Finally, the Office Action states that Cheung teaches methods for detecting EBV nucleic acid using an amplification method involving primers/probes that are 19-21 nucleotides in length. The Office Action concludes that it would have been obvious to "have generated additional probes to the EBV BARF-1 sequences and to have generated primers for amplifying BARF-1 sequences in order to have provided an effective means for amplifying and detecting the expression of BARF-1 sequences." (Office Action, page 14, para. 3, lines 1-5). This rejection is respectfully traversed below.

The inventors have discovered that the recited oligonucleotides may be used as amplification primers to amplify particular regions of the BARF-1 open reading frame spanning nucleotides 165504 – 166166. Alternatively, the sequences may be used as probes to detect the BARF-1 sequences. The

inventors have further made the discovery that expression of this open reading frame of the BARF-1 region is diagnostic of EPV-positive nasopharyngeal carcinoma and gastric carcinoma as opposed to other EBV-positive diseases.

None of the cited references, taken alone or in any combination, provide any motivation to one of ordinary skill in the art to select amplification primers and probes specific to the recited open reading frame of the BARF-1 region. It is therefore asserted that the claimed invention is nonobvious over NCBI in view of Zhang and Cheung, and respectfully requested that the outstanding rejection under § 103(a) be withdrawn.

G. NCBI (Accession No. M80517) in view of Zhang et al. and Cheung et al. and Kievits.

Claims 21 and 22 stand rejected under 35 U.S.C. § 103(a) as unpatentable for obviousness over NCBI (Accession No. M80517) in view of Zhang et al. and Cheung et al. and further in view of Kievits. The NCBI, Zhang et al. and Cheung et al. references have been discussed above. The Office Action states that Kievits further teaches a method for amplifying nucleic acids by NASBA with primers modified to include a T7 polymerase promoter sequence at the 5' terminus. This rejection is respectfully traversed below.

As discussed in the preceding section, the present inventors have discovered that the recited region of the BARF-1 region may be used as a diagnostic tool to identify EBV-positive NPC and gastric carcinoma. There is no suggestion or motivation of any kind in the cited references to so use the recited oligonucleotides. Accordingly, the subject matter of Claims 21 and 22 is nonobvious over the cited references, taken alone or in any combination, and it is respectfully requested that the outstanding obviousness rejection be withdrawn.

VIII. Conclusions.

The points and concerns raised in the Office Action having been addressed in full. It is respectfully submitted that this application is in condition for allowance, which action is respectfully requested. Should the Examiner have any remaining concerns, it is requested that the Examiner contact the undersigned attorney to expedite the prosecution of this application.

Respectfully submitted,

Karen A. Magri
Registration No. 41,965

Enclosure: Duplicate Paper Copy of the Sequence Listing

Customer No.

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, Washington, DC 20231, on December 3, 2002.

Sloan Hobbs

Version with Markings to Show Changes Made

In the Specification.

Please amend the paragraph on Page 7, line 29 through Page 8, line 16 as follows:

A more preferred embodiment of the present invention is directed to a pair of oligonucleotides, for the amplification of a target sequence within a Epstein Barr virus sequence, for use as a set, comprising:
1.2, 5'-CTCCCTTTACAACCTAAGGC-3' [SEQ.ID.NO.: 2], and
2.1, 5'-AGAGACAAGGTCCTTAATCGCATCC-3' [SEQ.ID.NO.: 3] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37] (EBNA-1);
or
1.1, 5'-CGGGCGGACCAGCTGTACTTGA-3' [SEQ.ID.NO.: 6] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37], and
2.2, 5'-GAGGTTTTGATAGGGAGAGGAGA-3' [SEQ.ID.NO.: 7] (EBER-1);
or
1.1, 5'-ATACCTAAGACAAGTTTGCT-3' [SEQ.ID.NO.: 12] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37], and
2.1, 5'-CATCGTTATGAGTGACTGGA-3' [SEQ.ID.NO.: 14] (LMP-1);
or
1.2, 5'-aggtactcttggtgcagccc-3' [SEQ.ID.NO.: 18], and
2.1, 5'-agcatataggaacagtcgtgcc-3' [SEQ.ID.NO.: 19] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37] (LMP-2);
or
1.2, 5'-ggctgtcaccgctttcttgg-3' [SEQ.ID.NO.: 23], and

2.1, 5'-agtgttggcacttctgtgg-3' [SEQ.ID.NO.: 24] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37] (BARF-1);

or

1.1, 5'-TGGAGCGAAGGTTAGTGGTC-3' [SEQ.ID.NO.: 27], and

2.2, 5'-AGACATGGTCTTTGGCTTCAGGGTC-3' [SEQ.ID.NO.: 30] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37] (vIL10 (BCRF1));

or

1.1, 5'-CTACCTTCCACGACTTCACC-3' [SEQ.ID.NO.: 32] provided with a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' [SEQ.ID.NO.: 37] and

2.1, 5'-AGGCCATGGTGTCATCCATC-3' [SEQ.ID.NO.: 34], or

2.2, 5'-AGAGAGAGAGTAGGTCCGCGG-3' [SEQ.ID.NO.: 35] (BDLF2).

In the Claims.

Please amend the claims as follows:

15. (Amended) A method for determining the presence of EBV-positive nasopharyngeal carcinoma or gastric carcinoma [epithelial tumor] cells in a sample of an individual suspected of or at risk for carrying an EBV associated disease, comprising:

(a) [-determining the presence of EBV positive cells by] amplifying one or more targets from [at least one RNA selected fro the group consisting of:

-]the BKRF1 reading frame spanning nucleotides 107950 – 109872 of EBNA-1[, and
- a target within exons 2, 3, 4, 5, 6, 7 and 8 spanning nucleotides 58 - 272, 360 - 458, 540 - 788, 871 - 951, 1026 - 1196, 1280 - 1495 and 1574 – 1682, respectively, of LMP-2],

(b) [-said method further comprising] amplifying one or more target sequence(s) selected from the BARF1 reading frame spanning nucleotides 165504 –166166,

(c) detecting the presence or absence of the amplified target sequences of steps (a) and (b), and

(d) determining the presence of EBV-positive nasopharyngeal carcinoma or gastric carcinoma [epithelial tumor] cells from the presence of the amplified target sequences of steps (a) and (b).

16. (Amended) The method according to claim 15 wherein [the pairs of oligonucleotides used in the amplification of the respective RNA(s) are selected from the group consisting of:]

-the step of amplifying the BKRF1 reading frame in step (a) is performed using a pair of oligonucleotides, each oligonucleotide comprising a sequence specific for **EBNA-1**, the EBNA-1 specific sequences consisting of

5'-CTCCCTTTACAACCTAAGGC-3' [SEQ.ID.NO.: 2], and

5'-AGAGACAAGGTCCTTAATCGCATCC-3' [SEQ.ID.NO.: 3],

[provided with] wherein the latter oligonucleotide further comprises a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' (**SEQ ID NO:37**);

and

- the step of amplifying the BARF1 reading frame in step (b) is performed using a pair of oligonucleotides, each oligonucleotide comprising a sequence specific for **BARF-1**, the BARF-1 specific sequences consisting of

5'-GGCTGTCACCGCTTTCTTGG-3' [SEQ.ID.NO.: 23], and

5'-AGTGTTGGCACTTCTGTGG-3' [SEQ.ID.NO.: 24],

[provided with] wherein the latter oligonucleotide further comprises a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' (**SEQ ID NO:37**).

19. (Amended) An oligonucleotide[, corresponding to part of a nucleic acid sequence encoding Epstein Barr Virus, said oligonucleotide being] that is 15-35 [10-35] nucleotides in length comprising at least a fragment of 15 [10] nucleotides of [a sequence selected from the group consisting of:

-the BKRF1 reading frame spanning nucleotides 107950 - 109872 of EBNA-1, and

-]the BARF1 reading frame spanning nucleotides 165504 –166166 and sequences complementary thereto.

20. (Amended) The oligonucleotide according to claim 19, being 15-35 [10-35] nucleotides in length comprising at least a fragment of 15 [10] nucleotides of the [a] sequence [selected from the group consisting of:

-5'-GCCGGTGTGTTGTTCGTATATGG-3' [SEQ.ID.NO.: 1], (**EBNA-1**),

-5'-CTCCCTTTACAACCTAAGGC-3' [SEQ.ID.NO.: 2], (**EBNA-1**),

-5'-AGAGACAAGGTCCTTAATCGCATCC-3' [SEQ.ID.NO.: 3], (**EBNA-1**),

-5'-AATACAGACAATGGACTCCC-3' [SEQ.ID.NO.: 4], (**EBNA-1**),

- 5'-CAGGTTCATCGCTCAGCTCC-3' [SEQ.ID.NO.: 22], (**BARF-1**),]

- 5'-GGCTGTCACCGCTTTCTTGG-3' [SEQ.ID.NO.: 23], (**BARF-1**)[,

- 5'-AGTGTTGGCACTTCTGTGG-3' [SEQ.ID.NO.: 24], (**BARF-1**), or

- 5'-AGCATGGGAGATGTTGGCAGC-3' [SEQ.ID.NO.: 25], (**BARF-1**),]

and sequences that are [their] complementary thereto [sequences].

23. (Amended) A pair of oligonucleotides, for the amplification of a target sequence within an Epstein Barr virus sequence, for use as a set, each oligonucleotide comprising an Epstein Barr virus sequence selected from the group consisting of [comprising]:

(a) 5'-CTCCCTTTACAACCTAAGGC-3' [SEQ.ID.NO.: 2], and 5'-AGAGACAAGGTCCTTAATCGCATCC-3' [SEQ.ID.NO.: 3], [provided with] wherein the latter oligonucleotide further comprises a T7

polymerase promoter sequence 5'-aattctaatacgactcactataggg-3'(**SEQ ID NO:37**) (**EBNA-1**);

and [or]

(b) 5'-GGCTGTCACCGCTTTCTTGG-3' [SEQ.ID.NO.: 23], and 5'-AGTGTTGGCACTTCTGTGG-3' [SEQ.ID.NO.: 24], wherein the latter oligonucleotide further comprises [provided with] a T7 polymerase promoter sequence 5'-aattctaatacgactcactataggg-3' (**SEQ ID NO:37**) (**BARF-1**).

24. (Amended) An oligonucleotide according to claim 19, being 15-35 [10-35] nucleotides in length comprising at least a fragment of 15 [10] nucleotides of the sequence [selected from the group consisting of:

5'-CGTCTCCCCTTTGGAATGGCCCCTGGACCC-3' [SEQ.ID.NO.: 5] (**EBNA-1**), provided with a detectable label; or]

5'-CTGGTTTAAACTGGGCCCAGGAGAGGAGCA-3' [SEQ.ID.NO.:26] (**BARF1**) [, provided with a detectable label] ,

and sequences that are complementary thereto.

25. (Amended) A test kit for performing a [the] method [of claim 15] for determining the presence of EBV-positive nasopharyngeal carcinoma or gastric carcinoma cells in a sample of an individual suspected of or at risk for carrying an EBV associated disease, the test kit comprising:

-one or more oligonucleotides according to any of claims 19-22, 24 and 29, 30, 32 and 33,

[-an oligonucleotide comprising a nucleic acid sequence substantially complementary to at least part of the amplified nucleic acid sequence, provided with a detectable label,] and

-suitable amplification reagents.

26. (Amended) A test kit according to claim 28 [24], wherein said oligonucleotide probe [that is provided with a detectable label is an

oligonucleotide being] is 10-35 nucleotides in length and comprises [comprising] at least a fragment of 10 nucleotides of the sequence set forth as 5'-CTGGTTTAAACTGGGCCCAGGAGAGGAGCA-3' [SEQ.ID.NO.: 26] (**BARF1**) linked to the detectable label.

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